3D Proton MR Spectroscopic Imaging of Prostate Cancer: Accuracy Evaluation in Different Prostate Regions

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Introduction/Purpose: The three dimensional magnetic resonance spectroscopic imaging (3D-MRSI) of prostate suffers from spatially dependent effects such as inhomogenous static magnetic field, spectral contamination from lipids, inhomogenous sensitivity of endorectal coil and motion artifacts. As a result of it, spectral quality and accuracy of fitted (choline+creatine)/citrate (CC/C) ratios substantially vary within measured 3D-MRSI data set. Therefore we evaluated routine 3D-MRSI protocol in the patients suspicious for prostate cancer and compared the accuracy of this method between the different prostate regions and measurement resolutions. Moreover, metabolic-quality maps as an effective way to present 3D-MRSI results by combing metabolic and error information in one image [1] are also demonstrated.

Subjects and Methods: From 29 subjects with a median age of 64 years (range 38 to 77) included in this study, 12 had positive prostate biopsy findings with median Gleason score of 3+3 (range 3+3 to 5+5). All MR measurements were done on a 1,5T Siemens Avanto whole body system (Siemens, Erlangen, Germany). Body coil served for RF transmission and a combination of endorectal (ER) coil (Medrad, Pittsburgh, PA, USA) with spine- and body-phased array coils were used for signal reception. At first the series of localizers for proper positioning of the ER coil and high-resolution transversal and coronal T_2-weighted turbo spin-echo images were recorded from prostate and seminal vesicles. The PRESS sequence optimized for detection of prostate cancer [2] was employed with the following parameters: TR/TE = 650/120 ms, bandwidth of 1400 Hz, 512 complex data points, 12 averages, elliptically sampled *k*-space filtered with 100% Hanning and 12x10x10 phase encoding steps acquired in 11:23 min. Due to different prostate sizes, the measurements were done with nominal voxel size of 6x6x6 (n=17) or 7x7x7 mm^3 (n=12). Semi-automated shimming procedure using field maps revealed mean line-width of water peak of 18.3 Hz (range 14.2 to 24.6 Hz).

$$\delta_{CCC} = \sum_{i=1}^{4} \frac{100 \cdot \left|\frac{\partial q}{\partial x_i}\right| \cdot \delta x}{A_i} \quad \text{(Eq.1)}$$

Pre-processing and quantification of 3D-MRSI data was performed in jMRUI software package [3]. By fitting spectra using AMARES with appropriate prior knowledge [4], the integrals of choline, creatine and two citrate inner lines with corresponding Cramér-Rao lower bounds (CRBs) were estimated. Those were exported in output files and evaluated in the built-in-house software written in Microsoft Visual Basic (Microsoft Corp.) Total inaccuracy of CC/C ratio (δ_{CCC}) normalized by its value and expressed in percentage was calculated according to equation 1, where function q describes the division of metabolites x_i in the ratio, δx_i are CRBs of the corresponding metabolites, A_i is the metabolite amplitude and index i runs through all N estimated amplitudes in the ratio q. For the evaluation of 3D-MRSI accuracy, each prostate data set was divided into base (blue), mid-gland (yellow) and apex (red) section (Fig.1a) in head-feet direction. From each section one representative 3D-MRSI slab was chosen and divided according to tissue type into peripheral (yellow) and central zone voxels (red) (Fig.1b) and based on the voxels position within the prostate into inner (red) and outer voxels (yellow) (Fig1c).

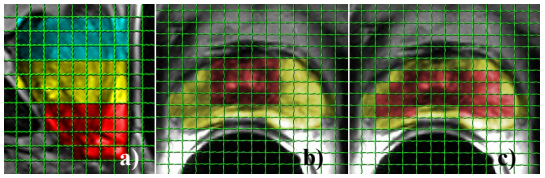

Fig.1: Prostate division to: a) sections, b) zones, c) voxels.

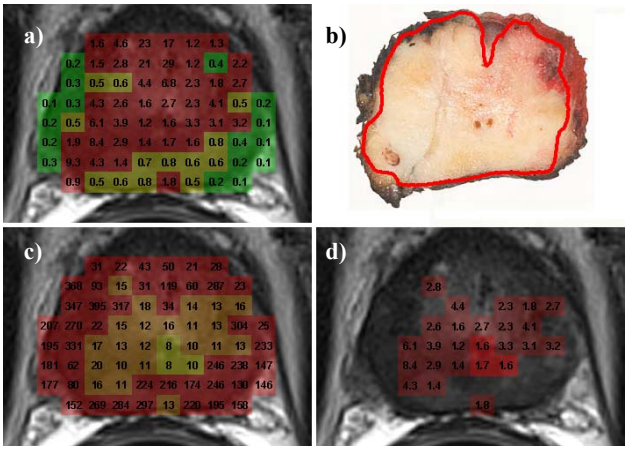

Fig.2: a) Metabolic CC/C ratios map. b) Histopathologic area of cancer. c) Map of CC/C inaccuracies d) Metabolic-quality map of CC/C ratios.

Results: 5347 voxels in 86 MRSI slabs were evaluated. Metabolic maps of CC/C ratios overlaid on the corresponding T2 images were created, where green voxels mark healthy, yellow suspicious and red cancerous tissue (Fig.2a). Similarly, maps of CC/C ratios inaccuracies with the least inaccurate voxels in yellow and the most inaccurate in red (Fig.2c) were produced. For effective presentation of 3D-MRSI results metabolic-quality maps were created. Here, the transparency of each voxel in metabolic CC/C ratio map was adjusted according to corresponding inaccuracies in CC/C ratio (Fig.2d) [1]. Voxels with CC/C inaccuracies in the interval of 0-10% were displayed as less transparent than voxels from the interval of 10-20%. Voxels with CC/C inaccuracies higher than 20% were set totally transparent. The cut-off value of 20% as a limit for acceptable accuracy has already been used in many approaches [5]. As it can be seen on figure 2, although the metabolic map also revealed healthy voxels (Fig.2a), after excluding the voxels with inaccuracies higher than 20% (Fig.2d), only cancerous voxels left. This corresponds with the spread of cancer from the histological findings (Fig.2c) and the pT4a stage (Gleason score of 5+5).

Four-way ANOVA for repeated measures with random factor found significantly more accurate CC/C ratios in 7x7x7 mm^3 voxels than in 6x6x6 mm^3 voxels (p=0.001) (Fig.3a). Significantly less precise CC/C ratios were found in prostate base than in apex (p<0.001) and middle gland (p<0.001) (Fig.3a). The accuracy of CC/C ratios in inner voxels was significantly higher than in outer voxels (p≤0.002) (Fig.3b). Although significantly less precise CC/C ratios were found in central than in peripheral zone for outer voxels (p<0.001), no significant difference between zones has been observed for inner voxels (Fig.3b).

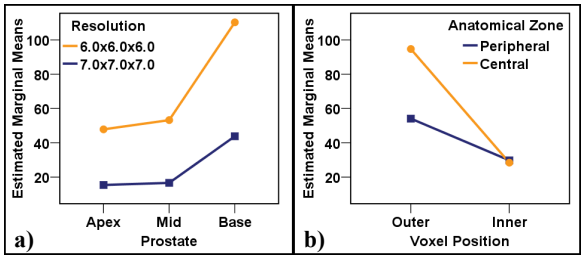

Fig.3: Comparison of estimated marginal means. a) Resolution of 6x6x6 vs. 7x7x7 and prostate apex vs. mid-gland vs. base. b) Peripheral vs. central zone voxels and outer vs. inner voxels.

Discussion/Conclusion: Although the 3D-MRSI measurements are applied for prostate cancer detection already for many years, to our best knowledge the accuracy of this method in different prostate regions have not been determined yet. Therefore we evaluated prostate 3D-MRSI in 29 patients and showed how measurement parameters and position of voxel of interest within the 3D-MRSI data set influence the accuracy of CC/C ratio. As our analysis suggests, the most accurate 3D-MRSI results can be found in the inner voxels of the prostate apex and mid-gland. On the other hand, the voxels from the prostate base and from the prostate periphery - outer voxels – suffer the most from inaccurate CC/C ratios. The reliability in this parts is mainly limited by the nearness of the bladder, air filled ER-coil and adipose tissue which hamper spectral quality and fitting accuracy. 3D-MRSI results from these prostate regions are often biased and could more often result in misleading findings.

The metabolic-quality maps, which present the information of CC/C ratio and its fitting accuracy in one image using the varying voxel transparency, were also presented. These maps enable fast and correct detection of prostate cancer without time consuming manual inspection of spectral quality in each prostate voxel. Moreover, it also allows accurate interpretation of 3D-MRSI findings without having any "knowledge" about the MR spectroscopy. Therefore we suggest to evaluate the accuracy of CC/C ratios in every voxel and/or use the metabolic-quality maps in order to refuse all unreliable data that could lead to incorrect diagnosis.

References: [1] Jiru, F., et al., *MAGMA*, 2006; 19(1): p. 1-14. [2] Scheenen, T.W.J., et al., *Magn Reson Med*, 2004; 52(1): p. 80-88. [3] Naressi, A., et al., *MAGMA*, 2001; 12(2-3): p. 141-52. [4] Vanhamme, L., et al., *J Magn Reson*, 1997; 129(1): p. 35-43. [5] Provencher, S.W., *Magn Reson Med*, 1993; 30(6): p. 672-9.